REMARKS

Claims 1, 5 and 21-25 are pending.

I. First Rejection under 35 U.S.C. §103

Claims 1, 5, and 21-25 are rejected under 35 U.S.C. §103(a) as being unpatentable over Stamler et al (US 6,472,390) in view of Adams et al (US 6,747,063) and over Goodman (US 6,087,398) in view of Loscalzo (US 6,635,273).

Applicants respectfully traverse the rejection and respectfully submit that the claimed invention is unobvious over the cited reference.

The pending claims 1, 5 and 21 are directed to the treatment of sickle cell anemia comprising administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate and at least one hydralazine compound.

Stamler is cited by the Examiner for the treatment of sickle cell anemia by the administration of a NO donor. Adams is cited by the Examiner in teaching that N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate are NO donors. As pointed out by the Examiner, neither Stamler nor Adams mention of the use of a hydralazine compound (i.e. antioxidant) either alone or in combination with a nitric oxide donor for the treatment of sickle cell anemia. Additionally there is no suggestion or motivation by Stamler or Adams to treat sickle cell anemia by administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with a hydralazine compound.

Goodman is cited by the Examiner for teaching methods of treating sickle cell anemia by administering an antioxidant. Goodman does not disclose or suggest of the use of a NO donor (i.e. N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate) either alone or in combination with a hydralazine compound (i.e. antioxidant) for the treatment of sickle cell anemia. Additionally, hydralazine compounds are structurally very different from N-acetyl cysteine, dithiothreitol, cysteamine, dimercaprol and succimer disclosed by Goodman (see, column 8, lines 64-65 and claim 2). Hence there is no motivation for one skilled in the art to use a hydralazine compound for the treatment of treating sickle cell anemia based on the teachings in Goodman.

Goodman does not cure the deficiencies of Stamler and Adams. Goodman does not provide any motivation or suggestion to modify Stamler and Adams to arrive at the claimed invention. In view thereof, Stamler and Adams in combination with Goodman do not motivate one to arrive at the present invention.

Loscalzo is cited by the Examiner for teaching that hydralazine and hydralazine compounds are known antioxidants. Applicants respectfully submit that Loscalzo does not disclose the treatment of sickle cell anemia by the administration of a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with hydralazine compounds. Additionally the vascular diseases disclosed by Loscalzo are very different from sickle cell anemia of the present invention. Moreover there is no suggestion or motivation by Loscalzo to treat sickle cell anemia by administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with a hydralazine.

Loscalzo does not cure the deficiencies of Stamler, Adams and Goodman. Loscalzo does not provide any motivation or suggestion to modify Stamler, Adams and Goodman to arrive at the claimed invention. In view thereof, Stamler and Adams in combination with Goodman and Loscalzo do not motivate one to arrive at the present invention.

Pending claims 22-25 are directed to the treatment of thalassemia comprising administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate and at least one hydralazine compound.

Stamler is cited by the Examiner for the treatment of thalassemia by the administration of a NO donor. Adams is cited by the Examiner in teaching that N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate are NO donors. As pointed out by the Examiner, neither Stamler nor Adams mention of the use of a hydralazine compound (i.e. antioxidant) either alone or in combination with a nitric oxide donor for the treatment of thalassemia. Additionally there is no suggestion or motivation by Stamler or Adams to treat thalassemia by administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with a hydralazine compound.

Goodman is cited by the Examiner for teaching methods of treating sickle cell anemia by administering an antioxidant. Goodman does not disclose or suggest of the use of a NO donor (i.e. N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate) either alone or in combination with a hydralazine compound (i.e. antioxidant) for the treatment of thalassemia. In fact Goodman does not even mention thalassemia. Moreover sickle cell anemia disclosed by Goodman is very different from thalassemia of the present invention. Additionally, hydralazine compounds are structurally very different from N-acetyl cysteine, dithiothreitol, cysteamine, dimercaprol and succimer disclosed by Goodman (see, column 8, lines 64-65 and claim 2). Hence Goodman is not analogous art. There is no motivation for one skilled in the art to use a hydralazine compound for the treatment of treating thalassemia based on the teachings in Goodman.

Goodman does not cure the deficiencies of Stamler and Adams. Goodman does not provide any motivation or suggestion to modify Stamler and Adams to arrive at the claimed invention. In view thereof, Stamler and Adams in combination with Goodman do not motivate one to arrive at the present invention.

Loscalzo is cited by the Examiner for teaching that hydralazine and hydralazine compounds are known antioxidants. Applicants respectfully submit that Loscalzo does not disclose the treatment of thalassemia by the administration of a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with hydralazine compounds. Additionally the vascular diseases disclosed by Loscalzo are very different from thalassemia of the present invention. Moreover there is no suggestion or motivation by Loscalzo to treat thalassemia by administering a therapeutically effective amount of N-hydroxy-L-arginine, isosorbide dinitrate or isosorbide mononitrate in combination with a hydralazine.

Loscalzo does not cure the deficiencies of Stamler, Adams and Goodman. Loscalzo does not provide any motivation or suggestion to modify Stamler, Adams and Goodman to arrive at the claimed invention. In view thereof, Stamler and Adams in combination with Goodman and Loscalzo do not motivate one to arrive at the present invention.

In view of the above, Applicants respectfully submit that the claims of the present invention are unobvious over the cited references, alone and in combination, and respectfully request the rejection under 35 U.S.C. §103(a) be withdrawn.

II. Conclusion

In view of the above amendment, Applicants believe the pending application is in condition for allowance.

Applicant believes no fee is due with this response. However, if a fee is due, please charge our Deposit Account No. 08-0219, under Order No. 0102258.00375US2 from which the undersigned is authorized to draw.

Respectfully submitted,

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/Belinda M. Lew/
Belinda Lew
Registration No.: 53,212
Attorney for Applicant(s)

Wilmer Cutler Pickering Hale and Dorr LLP
1875 Pennsylvania Avenue, NW
Washington, DC 20006
(202) 663-6000 (telephone)
(202) 663-6363 (facsimile)